Prophylactic Use of High-frequency Percussive Ventilation in Patients with Inhalation Injury

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Death and the incidence of pneumonia are significantly increased in burn patients with inhalation injury, despite application of conventional ventilatory support techniques. The effect of high-frequency percussive ventilation on mortality rate, incidence of pulmonary infection, and barotrauma were studied in 54 burn patients with documented inhalation injury admitted between March 1987 and September 1990 as compared to an historic cohort treated between 1980 and 1984. All patients satisfied clinical criteria for mechanical ventilation. High-frequency percussive ventilation was initiated within 24 hours of intubation. The patients' mean age and burn size were 32.2 years and 47.8%, respectively (ranges, 15 to 88 years; 0% to 90%). The mean number of ventilator days was 15.3 ± 16.7 (range, 1 to 150 days), with 26% of patients ventilated for more than 2 weeks. Fourteen patients (25.9%) developed pneumonia compared to an historic frequency of 45.8% ($p < 0.005$). Mortality rate was 18.5% (10 patients) with an expected historic number of deaths of 23 (95% confidence limits of 17 to 28 deaths). The documented improvement in survival rate and decrease in the incidence of pneumonia in patients treated with prophylactic high-frequency ventilation (HFV), as compared to a cohort of patients treated in the 7 years before the trial, indicates the importance of small airway patency in the pathogenesis of inhalation injury sequelae and supports further use and evaluation of HFV.

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D URING THE PAST three decades, improvements in burn wound management, infection control, and metabolic support increased the survival of thermally injured patients. Inhalation injury, however, continues to be a significant comorbid factor in such patients, and its treatment has been improved little by the use of conventional means of pulmonary support. Bac-

terial pneumonia, which historically occurred in 38% of all patients with inhalation injury but in only 8% of those without such injury, continues to be the leading cause of morbidity and death. The combination of inhalation injury and pneumonia exert independent but additive effects on the age-related death attributable to burn size.[1]

Current treatment for inhalation injury is supportive and includes aggressive pulmonary toilet, mechanical ventilatory support when indicated, and aggressive treatment of pneumonia when diagnosed. In an ovine model, we showed that the major insult after smoke injury (as indexed by early postinjury ventilation/perfusion (VA/Q) mismatching and histopathologic findings) is the obstruction and collapse of small airways leading to distal atelectasis and subsequent pneumonia.[2] Experimental and clinical data suggest that high-frequency ventilation (HFV) may be beneficial in recruiting and stabilizing such collapsed diseased lung segments.[3-12] In addition some investigators reported improved clearance of secretions from the tracheobronchial tree with the use of HFV.[13] These observations support the hypothesis that HFV, by preventing alveolar collapse and improving secretion clearance, may be beneficial in patients with inhalation injury.

We previously reported a small cohort of 10 patients with inhalation injury requiring mechanical ventilatory support in whom the prophylactic use of high-frequency percussive ventilation (HFPV) appeared to reduce the incidence of pneumonia.[14] This report extends our observations to 54 patients in whom HFPV was used in a prophylactic manner in an attempt to decrease the incidence of pneumonia and improve survival rate.

Methods

Patient Population

All adult patients admitted to the United States Army Institute of Surgical Research between March 1987 and September 1990 with a diagnosis of inhalation injury were eligible for enrollment in this study. Inhalation injury was confirmed in each patient by bronchoscopy and/or[133] Xenon ventilation–perfusion lung scan. The presence of carbonaceous debris beneath the true vocal cords, mucosal erythema, and ulceration were used to define moderate to severe inhalation injury. Patients with a positive[133] Xenon scan and negative bronchoscopy were determined to have mild inhalation injury. These criteria were established in our earlier review.[1] After meeting the entrance requirements listed in Table 1 and meeting the requirements for intubation and mechanical ventilatory support listed in Table 2, informed consent was obtained from each patient and HFPV initiated for pneumonia prophylaxis.

High-frequency Percussive Ventilation

Description of the high frequency percussive ventilator used in this study has been published.[14] Briefly, HFPV was delivered by a high-frequency pulse generator with gas from the high-frequency pulse generator delivered through a nongated sliding venturi to a standard endotracheal tube. The venturi entrains humidified gas from a fresh bias gas flow provided from the ventilator. The system combines serial high-frequency sub-dead space volume breaths with a variable inspiratory:expiratory (I: E) ratio. Periodic interruption of the high-frequency pulsatile flow is programmed to allow return of airway pressure to baseline continuous positive airway pressure (CPAP). The duration of the percussive phase and of the return to baseline phase are adjusted to manipulate oxygenation and CO_2 elimination. Peak airway pressure also can be varied independently to maintain CO_2 clearance. The frequency of sub-dead space breaths can range between 1.5 and 15 hertz. FIO_2 and PEEP are adjusted to maintain O_2 saturation greater than 90%.

All patients were placed initially on a conventional mechanical ventilator. In those patients intubated elsewhere, such support was of less than 24 hours duration, and all patients were converted to HFPV within 1 hour of admission. The patients intubated at our institution received conventional ventilation during admission processing but

TABLE 1. Study Entrance Criteria

Inhalation injury documented by bronchoscopy or Xenon lung scan
Clinical requirement for ventilatory support
Admission within 48 hours of injury
Older than 15 years

TABLE 2. Requirements for Mechanical Ventilatory Support

1. Respiratory rate > 35/min
2. Vital capacity < 15 mL/kg
3. Inspiratory force < 25 cm H_2O
4. PAO_2/FIO_2 < 200
5. PCO_2 > 50 mmHg
6. Vd/Vt > 0.6
7. Upper airway edema
8. PCO_2 < 50 mmHg but progressively increasing
9. Increased work of breathing

were converted to HFPV within 1 hour. After placing the patient on HFPV, standard ventilator settings were used as a baseline and then altered as indicated by arterial blood gas determinations, pulse oximetry, and end tidal CO_2 monitoring. The duration of the percussive phase was set at 2 seconds, with a rate of return to baseline approximately 2 less than the intermittant mandatory ventilation (IMV) setting required to maintain normal acid-base balance on conventional mechanical ventilation. Peak airway pressures were set at 5 cm H_2O less than those developed when a conventional volume-limited ventilator was set to deliver a tidal volume of 12 to 15 mL/kg. The FIO_2 and PEEP were maintained initially at the same levels as on conventional mechanical ventilation. The frequency of the sub-dead space tidal breaths was initially set at 10 hertz. After stabilization for approximately 30 minutes, arterial blood gas measurements were obtained and adjustments made as indicated. The goal of ventilator therapy was to maintain oxygenation and ventilation at the lowest possible peak airway pressure and fractional inspired oxygen concentration. Patients were weaned and extubated according to standard criteria.

Diagnosis of Pneumonia

The diagnosis of pneumonia was based on standard criteria used in this institution for the past decade. Patients with sputum leukocytosis (more than 25 white blood cells per high-power field), lack of oropharyngeal contamination (less than 10 squamous cells per high-power field), a predominant organism on culture, and an infiltrate on chest roentgenograms were diagnosed as having pneumonia.

Data Analysis

The incidence of pneumonia and death in the study patients was compared with predicted values based on two previous studies. The first predictor used relates burn size and age to death for all patients admitted to the Institute of Surgical Research between January 1980 and December 1986. The second predictor used as a basis for comparison relates burn size, age, the presence of inhalation injury and the occurrence of pneumonia to death

TABLE 3. *Burn Mortality Predictors*

Predicted Mortality (PM) $= \dfrac{e^Y}{1 + e^Y}$

I. Logistic equation relating burn size and age to mortality: 1980–1986

$Y = -4.8216 + 0.10299$ (PCTB) $- 0.18879$ (Age) $+ 0.50873$ (Age^2/100) $- 0.27915$ (Age^3/10,000)

II. Logistic equation relating burn size, age, inhalation injury, and pneumonia to mortality: 1980–1984

$Y = -3.4953 + 0.09589$ (PCTB) $- 0.1988$ (Age) $+ 0.4478$ (Age^2/100) $- 0.20314$ (Age^3/10,000) $+ 0.59056$ (II) $+ 0.92530$ (PNeu)

PCTB, percentage of total body surface burned.
II = -1.0 if inhalation injury absent; $+1.0$ if inhalation injury present.
PNEU, -1.0 if pneumonia absent; $+1.0$ if pneumonia present.

in patients admitted between 1980 and 1984. The incidence of pneumonia in this latter patient population also was used for comparison purposes. Solution of the logistic equations listed in Table 3 provide the exponents for use in calculating the two values for predicted death.

Results

Patient Population

Fifty-four patients meeting the entrance criteria were enrolled in the study. Routine demographic data are included in Table 4. Ten patients died, for a mortality rate of 18.5%. The distribution of patients by burn size demonstrates that 50% of the patients had burns ranging between 30% and 60% of the body surface, which is the group of patients in whom inhalation injury has been reported to have its greatest impact on death (Fig. 1). Segregation of the patients by outcome revealed the expected differences between the two groups (Table 5); nonsurvivors were older and had larger burns and a greater incidence of pneumonia. Fifty-two of the fifty-four patients were diagnosed as having inhalation injury by bronchoscopy. The two patients with negative bronchoscopy but positive ^{133}Xenon scans developed severe adult respiratory distress syndrome (ARDS) in the first postburn week, necessitating mechanical ventilatory support.
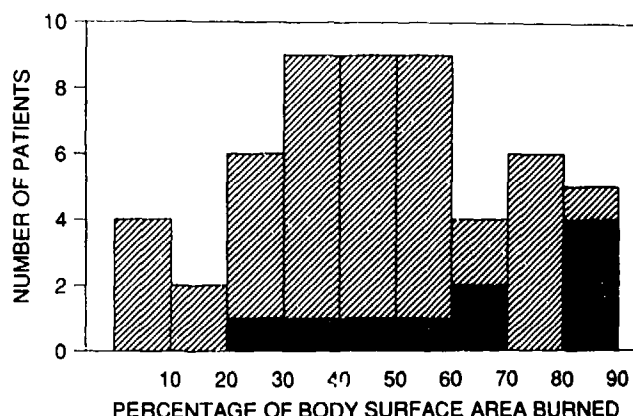

FIG. 1. Distribution of burn size for the 54 patients in the study. Of note is that 50% of the patient burn sizes are between 30% to 60% of the body surface area, which is the group of patients in whom inhalation injury exerts its greatest influence on mortality. Survivors are reported by the crossed bars, and nonsurvivors by the crosshatched bars.

Historically 45.8% of patients with positive bronchoscopy and 19.5% of patients with negative bronchoscopy but a positive ^{133}Xenon lung scan developed pneumonia. Based on that experience, 25 of the study patients would have been expected to develop pneumonia during hospitalization. Pneumonia was diagnosed in only 14 (26%) of the patients in this study, an incidence differing significantly from that of the comparison cohort (p < 0.003).

Actual Versus Predicted Death

Ten deaths occurred in this group of patients, for an observed mortality rate of 18.5%. To determine whether HFPV influenced outcome in this group of patients, we compared this observed mortality rate with two mortality predictions generated from patient data from this institution, as noted above. The first, based on burn size and age, related death in all patients admitted to this institution between January 1980 and December 1986, predicts the deaths of 19 patients (35%) in the study population, with a 95% confidence interval of 13 to 25 deaths. The second, based on burn size and age, related death in conjunction with the additive effects of inhalation injury and pneumonia and generated from patient data between January 1980 and December 1984, predicts 23 deaths (42.6%) with

TABLE 4. *Demographic Data*

Age	32.2 ± 1.8 (15–88)*
TBSB	47.8 ± 3.1 (0–90)
Sex	40 male, 14 female
Days on ventilator	15.3 ± 2.2 (1–150)
Bronchoscopy positive	96.3%
Incidence of pneumonia	25.9%
Mortality	10/54 (18.5%)

* X ± SEM (range).
TBSB, total body surface burn.

TABLE 5. *Comparison of Survivors and Nonsurvivors*

	Survivors	Nonsurvivors	
Age (years)	29.6 ± 1.5*	43.3 ± 6.5	p < 0.05
TBSB	43.7 ± 3.2	65.3 ± 7.1	p < 0.01
Incidence of pneumonia	20.5%	50%	p < 0.05

* Mean ± SEM.
TBSB, total body surface burn.

a 95% confidence interval of 17 to 28 deaths. Thus the mortality rate in this cohort of patients was significantly less than that predicted by either technique (p < 0.05) (Table 6).

The causes of death in those patients who died are listed in Table 7. Of the 10 deaths, four were from pulmonary failure. One patient could not be ventilated and oxygenated and was changed to conventional ventilatory support with the same result. Three patients developed progressive pulmonary failure and died on postburn days 12, 43, and 50, respectively. Of the remaining 6 patients, 2 were resuscitation failures who died with severe inhalation injury, 1 patient extubated himself on postburn day 7 and died of cardiopulmonary arrest despite an emergency tracheostomy, and 1 patient was removed from the study by his attending surgeon. Two patients died from cerebrovascular accidents after they were extubated for 30 and 45 days, respectively.

Ventilator complications were rare. Two patients developed severe necrotizing tracheobronchitis. It could not be determined whether this was secondary to the ventilator or the disease process itself. Barotrauma occurred in three patients. Two developed significant subcutaneous emphysema and one patient developed bilateral pneumothoraces requiring tube thoracostomies.

Discussion

The combination of cutaneous thermal injury and inhalation injury results in a significantly higher mortality rate than that attributable to cutaneous thermal injury alone. This additive effect of inhalation injury on death is most apparent in patients in whom predicted mortality attributable to age and burn size ranges from 40% to 60%. Inhalation injury also results in a marked increase in the incidence of bacterial pneumonia. As previously stated, only 8.8% of patients with thermal injury but without inhalation injury develop pneumonia during their course of treatment. The presence of inhalation injury, whether diagnosed by bronchoscopy or [133]Xenon scan, historically resulted in a 38% incidence of pneumonia, and the combination of inhalation injury and pneumonia has an even more drastic effect on outcome, increasing the mortality rate by as much as 60%.[1]

TABLE 6. Actual Versus Predicted Outcome

Predictor	Predicted Deaths	95% CL	Observed
#1 (1980–1986)	19	13–25	10
#2 (1980–1984)*	23	17–28	10

* This predictor includes the impact that inhalation injury and pneumonia have on outcome.
CL, confidence level.

TABLE 7. Cause of Death

TBSB (%)	Age (years)	PBD	Cause of Death
90	32	01	Resuscitation failure
85	25	03	Resuscitation failure
59	40	07	Accidental extubation
36	59	40	Removed from study
47	29	50	SBE, CVA, 30 days after extubation
65	60	80	CVA, 45 days following extubation
89	25	12	Pulmonary failure
30	88	43	Pneumonia (Staph. aureus), pulmonary failure
64	49	01	Unable to ventilate
86	29	50	Pneumonia, Aspergillus wound infection

TBSB, total body surface burn; PBD, postburn day.

Ideally the optimal treatment of any disease should reverse the pathophysiologic process without causing further injury. When inhalation injury is severe enough to require conventional mechanical ventilatory support, such an outcome is not achieved. The pathophysiologic response to inhalation injury includes extensive tracheobronchial injury, which results in sloughing of the mucosal lining of the respiratory tract and leads to obstruction of small- and moderate-sized airways. In addition, the mucociliary transport mechanism is impaired, resulting in impaired clearance of secretions and the sloughed debris. Distal airway obstruction results in atelectasis and, in conjunction with the disruption of the endothelial and epithelial integrity of the alveolus, produces foci for the development of bacterial overgrowth and subsequent pneumonia. The combination of atelectasis, pneumonia, and airway obstruction produces significant derangement of ventilation–perfusion relationships.

Conventional mechanical ventilatory support does not reverse these processes, is not characterized by improved clearance of secretions, and may actually compound the existing injury.[15] Conventional volume-limited ventilation in patients with inhalation injury normally is instituted at a tidal volume of 12 to 15 mL/kg. With such a ventilatory setting, peak inspiratory pressures often are elevated during the resuscitative and fluid mobilization phase of care. Recently Tsuno[16] reported adverse pulmonary effects of volume-limited mechanical ventilation when peak inspiratory pressures exceed 30 cm of water in paralyzed, anesthetized healthy sheep. Animals ventilated with an FIO_2 of 40% and a tidal volume of 10 mL/kg, with peak inspiratory pressure less than 18 cm of water, showed no measurable deleterious changes in lung function or histopathology after 48 hours of support. Animals ventilated with larger tidal volumes, resulting in peak inspiratory pressures greater than 30 cm H_2O, demonstrated progressive deterioration in static lung compliance, functional residual capacity, and arterial blood gases. Severe pul-

monary atelectasis, increased wet lung weight, and an increase in the minimum surface tension of saline lung lavage fluid were noted at autopsy. These data indicate that even in normal healthy lungs, prolonged elevation of inspiratory pressures may result in injury.

If pneumonia develops after resuscitation, the requirement for increased inspired oxygen concentrations to achieve normoxia may result in increased pulmonary damage when infection is present. Coalson et al.[17] recently reported a synergistic effect of hyperoxia and infection resulting in significant pulmonary dysfunction and damage. In a primate model, the combination of 80% O_2 and Pseudomonas pneumonia was as injurious as 100% oxygen during an 11-day period, while 80% O_2 or pneumonia alone resulted in minimal dysfunction.

The reported beneficial effects of HFV (ventilator frequency greater than 60 breaths/minute and tidal volumes of less than anatomic dead space) include lower peak airway pressures than those generated by conventional ventilation, positive endotracheal pressure throughout the ventilatory cycle, increased functional reserve capacity, and more efficient pulmonary gas distribution.[18] Unfortunately each of the advantages claimed for specific high-frequency ventilators has been refuted in various reports.[9,10,12] If, however, a form of HFV could achieve some of these advantages and maintain oxygenation and CO_2 clearance at lower inspiratory pressures and fractional inspired concentrations of oxygen, it might be possible to provide ventilatory support and avoid the deleterious side effects of conventional support.

In evaluating clinical reports of HFV, the physician must recognize that there are several types of high-frequency ventilators, all with different characteristics and different potentially adverse effects. Furthermore one must differentiate between prophylactic use of the ventilator, as in this study, and therapeutic or salvage use of the high-frequency device for patients in whom conventional mechanical ventilatory support has failed. Many reports documented the effectiveness of short-term salvage use of HFV in patients with ARDS.[7,8] Our own previously reported experience demonstrated that the ventilator used in these studies could oxygenate and ventilate patients at lower airway pressures and inspired oxygen concentrations, but all the patients died despite improved pulmonary performance.[14] Other reports also failed to identify a survival advantage with the use of HFV as a salvage mode of ventilatory support.

In this study we used HFPV prophylactically in an attempt to avoid the adverse effects of mechanical ventilatory support while reversing or minimizing some of the pathophysiologic changes that occur after inhalation injury. Our data indicate that, as compared to a recent historic cohort, the use of HFPV resulted in a significant decrease in the incidence of pneumonia and a decrease in the number of deaths.

There are several problems inherent to the use of historic controls. The development of more sensitive diagnostic techniques resulting in the diagnosis of less severe injury could favorably bias the results of recent studies, although the diagnostic modalities and criteria have remained constant since 1976. It is generally accepted that during the past three decades, survival of all patients with thermal injury has improved. Even so the effects of inhalation injury and pneumonia on outcome have remained refractory to standard treatment, as indicated by the mortality predictor used at this institution. Furthermore the predictors used in this study introduce some bias against finding an improvement in outcome in the current study population as compared to the populations on which the predictors were based. The predictor that account for the effects of both burn size and age as well as pneumonia and inhalation injury on death was based on all patients with inhalation injury admitted during the years 1980 to 1984, regardless of whether they required mechanical ventilatory support. The present study population includes only the sickest patients with the most significant injuries, all requiring ventilatory support. Demonstration of a survival advantage in this group of patients compared to a group that included patients with less severe injury supports the hypothesis that HFPV has a significant, beneficial effect. In short it seems reasonable to assign a major portion of the decrease in incidence of pneumonia and improvement in outcome of the study patients to the ventilatory support used.

Only two other published studies in the literature evaluated the prophylactic use of HFV in patients requiring ventilatory support as prophylaxis against ARDS. In 1986 Carlon[18] reported a study of 309 patients who were randomized to high-frequency jet ventilation or conventional ventilatory support. All patients who were admitted to the intensive care unit and who were at risk for the development of pulmonary failure were entered into the study. The use of high-frequency jet ventilation resulted in lower peak airway pressures but did not decrease the 4% incidence of barotrauma or improve the overall outcome as compared to conventional support. In 1990 Hurst et al.[19] reported a study of 113 patients at risk for the development of ARDS who were randomized to receive ventilatory support with HFPV or conventional mechanical ventilation before the onset of ARDS. Changes in ventilator settings were made to achieve the same therapeutic endpoints in both groups of patients. There was no difference in the percentage of patients who developed ARDS in either group. In the patients who developed ARDS, HFV achieved therapeutic endpoints at lower peak airway pressures, lower positive end expiratory pressures,

and an increased inspiratory time as compared to the conventional group. There was, however, no difference in the incidence of barotrauma or outcome in those patients. Both of these studies involved heterogeneous patient populations, in which the etiology of respiratory failure was diverse, usually a consequence of a systemic insult that resulted in diffuse parenchymal disease and dysfunction. This type of insult is quite distinct from that seen after smoke inhalation in both humans and animal models, in which edema resolves rapidly after resuscitation and repair of the airway mucosa typically occurs within 14 to 21 days.

The exact mechanism by which HFPV achieved the results reported in this study is not known. We hypothesize that the ability to maintain ventilation and oxygenation at lower peak airway pressures and inspired oxygen concentrations may decrease the iatrogenic injury that occurs with conventional mechanical ventilatory support. Extrapolation of the data reported by Tsuno[16] to humans would indicate that ventilation at lower peak airway pressures offers significant advantage, especially in lungs that have already been injured. In addition several studies now suggest that asymmetric high-frequency breaths improve clearance of secretions, results that have been obtained with high-frequency jet ventilators and high-frequency oscillators, both *in vitro* and *in vivo*.[13,20-22] Our clinical experience supports this finding. Patients with severe inhalation injury treated prophylactically with high-frequency percussive ventilation typically are found, by bronchoscopic examination, to have large deposits of secretions at the tip of the endotracheal tube. After removal of these secretions, the main stem bronchi and distal airways often are patent and free of pathologic secretions. The documented improvement in survival and the decrease in the incidence of pneumonia in patients treated with prophylactic HFPV, as compared to the recent historic cohort, indicate the importance of maintaining small airway patency in reducing the sequela of inhalation injury. The beneficial effects reported here and the paucity of ventilator complications support continued use and further evaluation of HFV in patients with inhalation injury.

References

1. Shirani KZ, Pruitt BA Jr, Mason AD Jr. The influence of inhalation injury and pneumonia on burn mortality. Ann Surg 1987; 205: 82–87.
2. Shimazu T, Yukioka T, Hubbard G, et al. Frequency of VA/Q rates following smoke inhalation. USAISR Annual Research Progress Report 1985.
3. Bland Rd, Kim MH, Light MJ, et al. High frequency mechanical ventilation in severe hyaline membrane disease. Crit Care Med 1980; 8:275–280.
4. Brichant JF, Rouby JJ, Viars P. Intermittent positive pressure ventilation with either positive end expiratory pressure or high frequency jet ventilation (HFJV), or HFJV alone in human acute respiratory failure. Anesth Analg 1986; 65:1135–1142.
5. Butler WJ, Bohn DJ, Bryan AC, et al. Ventilation by high frequency oscillation in humans. Anesth Analg 1980; 59:577–584.
6. El-Baz N, Faber LP, Doolas A. Combined high frequency ventilation for management of terminal respiratory failure: a new technique. Anesth Analg 1983; 62:39–49.
7. Hurst JM, Branson RD, DeHaven CB. The role of high frequency ventilation in post-traumatic respiratory insufficiency. J Trauma 1987; 27:236–242.
8. Hurst JM, DeHaven CB. Adult respiratory distress syndrome: improved oxygenation during high frequency jet ventilation/continuous positive airway pressure. Surgery 1984; 96:764–769.
9. Jibelian G, Lachmann B. Gas exchange during conventional and high frequency pulse ventilation in the surfactant deficient lung: influence of positive and expiratory pressure. Crit Care Med 1984; 12:769–773.
10. Kaiser KG, Davies NJ, Rodriguez R, et al. Efficacy of high frequency ventilation in presence of extensive ventilation perfusion mismatch. J Appl Physiol 1985; 58:996–1004.
11. Kolton MK, Cattran CB, Kent G, et al. Oxygenation during high frequency ventilation compared with conventional mechanical ventilation in two models of lung injury. Anesth Analg 1982; 61: 323–332.
12. Kumar BS, Beney K, Jastremski M, et al. High frequency jet ventilation versus conventional ventilation after surfactant displacement in dogs. Crit Care Med 1984; 12:738–741.
13. Freitag L, Long WM, Kim CS, Wanner A. Removal of excessive bronchial secretions by asymmetric high-frequency oscillations. J Appl Physiol 1989; 67(2):614–619.
14. Cioffi WG, Graves TA, McManus WF, Pruitt BA Jr. High-frequency percussive ventilation in patients with inhalation injury. J Trauma 1989; 29(3):350–354.
15. Mammel MC, Boros SJ. Airway damage and mechanical ventilation: a review and commentary. Pediatr Pulm 1987; 3:443–447.
16. Tsuno K, Prato P, Kolobow T. Acute lung injury from mechanical ventilation at moderately high airway pressures. J Appl Physiol 1990; 69(3):956–961.
17. Coalson JJ, King RJ, Winter VT, et al. O₂—and pneumonia-induced lung injury I. Pathological and morphometric studies. J Appl Physiol 1989; 67(1):346–356.
18. Carlon GC, Howland WS, Ray C, et al. High-frequency jet ventilation—a prospective randomized evaluation. Chest 1983; 84(5): 551–559.
19. Hurst JM, Branson RD, Davis K Jr, et al. Comparison of conventional mechanical ventilation and high-frequency ventilation. Ann Surg 1990; 211(4):486–491.
20. Hachenberg T, Wendt M, Deitmer T, Lawin P. Viscoelasticity of tracheobronchial secretions in high-frequency ventilation. Crit Care Med 1987; 15(2):95–98.
21. Freitag L, Kim CS, Long WM, et al. Mobilization of mucus by airway oscillations. Acta Anaesthesiol Scand 1989; 33(Suppl 90): 93–101.
22. Thangathurai D, Holm AP, Mikhail M. et al. HFV in management of a patient with severe bronchorrhea. Resp Mgmt 1988; Jan/ Feb:31–33.

DISCUSSIONS

DR. HARVEY SUGERMAN (Richmond, Virginia): In this study, high-frequency percussive ventilation from 1987 through 1990 was associated with a significant decrease in, one, the incidence of pneumonia and, two, the mortality rate when compared, as mentioned, to historical controls for inhalational injury from 1980 through 1984 and mortality rate from 1980 through 1986.

As discussed in their paper, this is one of the only studies in which high-frequency ventilation has shown a significant decrease in mortality rate. It has been my experience and that of the literature that you can significantly, but only temporarily, improve blood gas parameters in ARDS patients with high-frequency ventilation. It prolongs death rather than improving survival.

The hypothesis proposed by Dr. Cioffi and his colleagues and supported by sheep inhalational injury studies in their laboratory is that high-frequency percussive ventilation improves bronchiopulmonary toilet of the small airways, which are plugged with soot and debris, with an increased alveolar recruitment and ventilation at lower peak airway pressures when high-frequency ventilation is provided early or prophylactically before the development of severe ARDS.

This has not been the case in nonburn septic patients in randomized prospective trials. Dr. Cioffi's study suffers from all of the potential weaknesses of a nonrandomized trial. In comparing inhalational injury and the risk of pneumonia, why did the authors compare data from 1980 to 1984 with 1987 to 1990?

What happened to the missing 3 years? Were other treatment modalities that could influence the development of pneumonia during these two time intervals changed, such as the use of H2 blockers versus carafate for the prevention of stress ulcers or TPN versus enteral feedings vis-a-vis the issue of bacterial translocation, and so on?

Were the methods of providing pulmonary toilet in the two groups, such as the nursing staff and inhalational therapists, unchanged during these two time periods?

Could prejudice have been inadvertently present in roentgenographic interpretation or were so-called blinded radiologists used to describe the presence or absence of pulmonary infiltrates?

Finally, using historical controls, were there any differences in the duration of mechanical ventilation versus duration of ventilation with high-frequency ventilation present?

We heard the duration of ventilation for high-frequency ventilation but not for the mechanical ventilatory group.

In 1988 this group reported their first positive experience with high-frequency percussive ventilation in 14 patients before the American Association for the Surgery of Trauma. Today we have heard more suggestive data in an additional 40 patients.

High-frequency ventilation has been a technique in search of documented therapeutic efficacy. Now is the time for a truly randomized prospective, perhaps multi-center trial for the study of high-frequency ventilation in burn inhalational injury patients.

Dr. DAVID HERNDON (Galveston, Texas): Dr. Cioffi and Dr. Pruitt and their group must be commended on their impressive mortality statistics. A mortality rate as low as 18.5% in a group of patients with significant inhalation and burn injury requiring prolonged ventilatory support has never been reported in the United States before.

The usual mortality rates quoted are from 40% to 50%. This in respect to nationally reported mortality rates is clearly a great advance and allows Brooke still to be called the world's most famous burn unit.

However demonstration of a treatment effect in a patient population with this high rate of mortality is extremely difficult. Comparison to an historic cohort from 1980 to 1984 or 1986 is somewhat misleading. The investigators have admitted that.

I would like to know if more aggressive early surgical removal of the burn wound in a later period may have contributed to a decrease in the incidence of pneumonia by decreasing burn wound bacteremia as a source of hematogenous pneumonia. Has there been any effect of the more recently developed antibiotics?

The H2 blockers have been mentioned.

You have noted also that a wide variety of high-frequency ventilators are available, and varying reports of efficacy in the literature have been received. The incidence of barotrauma, specifically pneumothoraces due to gas trapped behind inspissated mucosal casts, has been discouraging in inhalation injury patients. However the ventilator you used is very specific and seems to overcome many of these adverse effects with a very low incidence of barotrauma.

My major question is, is this complicated ventilator commercially available or will it become commercially available? I'm not aware of it being so. If it is, then I think, as Dr. Sugerman did, concurrent multicenter studies based on your encouraging preliminary results might be warranted to determine mortality effects, whether specific for this machine or specific for this excellent treatment team.

I would also like the authors to speculate as to whether our general level of burn care has improved to such an extent that we might also recontemplate randomized studies that would treat barotrauma by use of extracorporeal membrane oxygenation.

Previous attempts in the 1970s, when burn wound sepsis was rampant, were unsuccessful, but mortality statistics are sufficiently decreased, and early excision of the wound would prevent many of the septic complications that were seen before. Or perhaps the new technique of intravenacava filamentous O_2-CO_2 exchange rods being tested in multiple centers for support of adult respiratory distress syndrome might make more sense than a jet ventilator.

Dr. EDWIN DEITCH (Shreveport, Louisiana): I will limit my remarks to a few questions, some of which have been covered before but, nonetheless, I think they need to be stated again.

I wonder whether the authors are now ready to carry out a prospective randomized study to verify these results. There are several reasons to do so. The first is that this high-frequency ventilator technique that they are proposing is much more time consuming, technically demanding and more expensive than conventional mechanical ventilation.

And second, and perhaps more important, all too often in the past studies carried out using historical controls, even one as well defined as this one, fail to verify the encouraging results of the initial study.

There are many reasons why this phenomenon occurs, not the least of which is the special attention directed toward these patients by a highly motivated investigational team. Perhaps the fact that Dr. Cioffi and his coworkers were performing bronchoscopy on these patients to remove debris may have made this a study of repeated bronchoscopy as much as ventilatory support.

I have two other related questions. One is that it has become apparent in the last several years that the intubated patients receiving antacids or H2 blockers for stress ulcer have an increased incidence of gram-negative pneumonia and even death.

Therefore I wonder whether the authors are still using H2 blockers, what they're using, and whether they have changed their therapy to use sucralfate to prevent colonization of the stomach with potential pathogens.

Related to that, do you have any data on the bacteriology in these patients and if so was it different from the historical controls? I ask this question because pneumonia due to gram-negative enteric bacilli or pseudomonas is associated with a higher mortality rate than pneumonias caused by gram-positive organisms.

Therefore, if you are shifting your flora due to changes in therapy, you may also be shifting your results.

Dr. ANTHONY MEYER (Chapel Hill, North Carolina): I would like to compliment the authors on their continued evaluation of this alternate method of ventilation for inhalation injury. I have a few questions.

You had a relatively low incidence of necrotizing tracheobronchitis and barotrauma. Is this consistent with the incidence in your conventionally ventilated patients?

Is there any evidence or data on pulmonary compliance in these patients? Obviously it is difficult to measure using this mode of ventilation, but if pulmonary fibrosis is one of the key hallmarks of ARDS and late pulmonary problems, and if this is indeed triggered by the barotrauma of conventional ventilation, this might be a significant physiologic alteration using this type of support.

There is a relatively high incidence of pneumonia in the historical series. And because of this and many of the other reasons, I would like to join the chorus in suggesting that a true prospective randomized study should be carried out to evaluation further the technique.

I think it is interesting that this sophisticated pulmonary management is being discussed before a surgical society rather than something that is only discussed before pulmonary medicine groups.

DR. WILLIAM CIOFFI (Closing discussion): First I would like to address the recurring question of why we did not perform a randomized trial.

When we started this study, we did a trial in which we enrolled 20 patients to see if we could see a decrease in the incidence of pneumonia or change in mortality rate, and indeed we did. We entertained the thought of a prospective randomized trial at that time. By doing the calculations, we discovered that it would require more than 230 patients to have satisfactory type one and type two errors. It took us almost 4 years to enroll 54 patients in this trial, so we were looking at more than a decade to complete the study with all the problems that would occur in treatment changes in 10 years or more.

Second we have used these predictors for at least one decade in our institute, if not longer, and in other studies have found them to be entirely reliable in predicting results from other types of studies, not just including the ventilator study discussed here today.

Third because doing this randomized trial will be difficult in a period of time that is reasonable, we have begun a study in primates looking at high-frequency ventilation in two forms, high-frequency percussive ventilation discussed here today and high-frequency oscillation as compared to conventional ventilation in a long-term support model in which we ought to be able to discern whether the differences we see in patients will hold out in the primate model. That trial is now underway.

To continue with Dr. Sugerman's questions, other treatment modalities have not changed significantly in our unit in the past 10 years.

Our mode of nutritional support is enteral and has remained enteral for 10 years, with TPN being used in less than 5% of patients.

Our diagnosis and treatment of pneumonia also has remained the same in the studied period of 10 years.

Respiratory therapy has not changed significantly. Frequent bronchoscopy for pulmonary toilet in patients with severe inhalation injury has been the standard in the unit for approximately 10 to 15 years.

Dr. Sugerman also asked whether the duration of ventilatory support was similar in the high-frequency patients as compared to the conventional patients. Unfortunately I do not have that data for the 1980–1984 patients. But I would say that 15 days of support in these patients indicates a rather severe insult. The patients are weaned as quickly as possible from this ventilator, and it has been my experience in patients who have not been placed in the trial for other reasons that it is easier to wean the patients from high-frequency ventilation than conventional support.

Dr. Herndon asked about our excision practices. In the past decade, our day of first excision has decreased by about 3 days in patients with burn size discussed in this paper. He also asked whether the incidence of hematogenous *versus* bronchopneumonia or airway pneumonia has changed. Hematogenous pneumonia has been relatively infrequent in the past decade, and bronchopneumonia is responsible for almost all our pneumonias. I don't think that later excision in the earlier group had much to do with the incidence of pneumonia.

Our antibiotic therapy has been relatively unchanged. The standard antibiotic therapy in our unit is Amicacin and Vancomycin and has been that way for almost the entire period of the 1980s.

Several discussants asked about stress ulcer prophylaxis and whether we use H2 blockers. Until 5 or 6 months ago the standard of care was H2 blockers and antacids titrated to keep the gastric pH above 4.5.

We just started a trial comparing sucralfate to standard therapy, but of the patients reported in this study, only two of the last five patients were enrolled in that study. So all patients were on H2 blockers, and the idea of nonacid neutralizing therapy to decrease pneumonia does not enter into play.

The barotrauma reported in our series is low. It is lower than it has been in the past. The incidence of significant barotrauma as far as pneumothoraces was one patient of 54. Most ICUs report incidence of barotrauma approximately 4%. Two patients did have significant subcutaneous emphysema but never developed a pneumothorax.

Dr. Herndon asked whether this device was commercially available. It was approved by the FDA approximately 1 year ago and is now commercially available through Percussion Air Corporation, which is a company owned by Dr. Bird, who developed this form of ventilation.

Dr. Herndon also asked us to speculate whether other forms of support, total rest of the lungs using either ECCOR or the new intravenacaval device, the IVOX, might be of more benefit. In those studies it is still a requirement that the patient be kept on high mean airway, low peak pressure ventilation to splint the lung. And it might be that some high-frequency ventilation in combination with extracorporeal support might be the answer. The studies that are using that form of therapy, however, are all on ARDS patients.

Dr. Deitch asked not only about why not a prospective study, which I've already covered, but also about the costs. The cost of this ventilator is approximately one fifth of a 7200 ventilator. So cost is not really an issue.

The first two forms of this ventilator were exceptionally hard to use, as we reported in our early review; however the VDR for the most current form of this ventilation is very easy to use. We have residents who rotate 1 month from multiple institutions. And by the end of 1 month, most residents are capable of using this ventilator and are able to support the patients at night on their own.

Dr. Deitch also asked about the etiology of our pneumonia, our gram negatives *versus* gram positives. We have had a predominance of gram-positive pneumonias at our institute for more than a decade, and that incidence has not changed.

He also asked about comparing it to a population from 1980 to 1984 and 1987 to 1990. We are just starting to look at the data in the intervening years. And the incidence of pneumonia before use of this ventilation from 1985 to 1987 had not changed in patients with inhalation injury compared to the 1980 to 1984 group.

Finally Dr. Meyers asked about necrotizing tracheobronchitis. It is our impression that it has been significantly decreased with the use of this ventilator, despite the fact that there are reports in the literature using this form of ventilation in neonates, in which that incidence approaches one third to one half of patients.

However we only had two patients, the very first patient and a latter patient entered in the trial, both of whom survived. And it appeared to be more an indication of the severity of their insult.

Finally, Dr. Meyers, we have not done compliance measurements to indicate the severity of the insult.

In closing I would like to add that many discussants compared this form of support in patients with inhalation injury to those studies in the literature that deal with ARDS patients. I would emphasize that the insult in our patients is distinctly different from ARDS. It is a self-limiting disease process, which, if it can be left to heal on its own, should do so in 10 to 14 days. We feel strongly that conventional mechanical ventilatory support impairs that healing process and that the use of low-pressure ventilation by the use of this device or other high-frequency devices may just allow the natural process of healing to occur.